UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,515	06/16/2006	Francesca Frigerio	PC/4-32727A	9099

75074 7590 02/25/2009

NOVARTIS INSTITUTES FOR BIOMEDICAL RESEARCH, INC.
220 MASSACHUSETTS AVENUE
CAMBRIDGE, MA 02139

EXAMINER	
SWOPE, SHERIDAN	

ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
02/25/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,515	FRIGERIO ET AL.	
	Examiner	Art Unit	
	SHERIDAN SWOPE	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *1-11 and 17-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-16* is/are rejected.

7)☒ Claim(s) *12-16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' response of October 28, 2008, to the Action of May 28, 2008, is acknowledged. It is acknowledged that Claims 12 and 13 have been amended. Claims 1-26 are pending. Claims 1-11 and 17-26 were previously withdrawn from further consideration as being drawn to nonelected inventions. Claims 12-16 are hereby reexamined.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Double Patenting

Provisional rejection of Claims 12-16 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 13-17 of US Application US 10/568,637, for the reasons explained in the prior action, is maintained. Applicants state that, should it become necessary, they would consider obviating this [rejection] by filing a terminal disclaimer.

Claim Objections

Objection to Claims 12-16, for reciting non-elected subject matter, is maintained. Applicants are reminded that the elected invention is directed to a method of treating obesity using an S6K kinase activity inhibitor.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the following reasons.

For Claims 12-16, the phrase "S6 kinase1" renders the claims indefinite. Neither the claims nor the specification define the structure or function of all "S6 kinase1" proteins. The specification states:

> '"S6K" or "S6 kinase" is used herein to encompass both S6K1 (p70 and p85) and S6K2 (see, for example, Genebank Accession No. M57428, AJ007938, AB019245, NM003952 and related sequences), although S6K1 is a preferred target. Exemplary functional equivalents (variants) or derivatives of S6K include molecules where S6K is covalently modified by substitution, chemical, enzymatic, or other appropriate means with a moiety other than a naturally occurring amino acid.'
>
> and
>
> "S6 kinase is a kinase that phosphorylates the ribosomal protein, S6. Deletion of the S6K1 gene (also known as p70/p85 S6K) in mice led to the identification of an S6K1 homologue, S6K2, which can partly compensate for S6K1 function biochemically to phosphorylate S6 (Shima et al., 1998, EMBO J., 17, 6649-6659)." [0004]

Said statements fail to define the structural or functional limitations for all encompassed "S6 kinases". The skilled artisan would not know the metes and bounds of the recited invention.

For Claim 12, the phrase "a weight disorder dependent on fat accumulation" renders the claim indefinite. The specification states: "...a method is provided for screening an agent effective in treating a weight disorders dependent on fat accumulation (e.g. obesity)..." (pg 9, parg 3). Said statement fails to define the phrase because (i) it fails to define the phrase "fat accumulation", which is a relative term, and (ii) it is only exemplary. The skilled artisan would not know the metes and bounds of the recited invention.

For Claim 13, the term "obesity" renders the claim indefinite. The description in the specification on how to determine whether a human is suffering from obesity (parg brdg pg 24-

25) is only exemplary and does not define the metes and bounds of the recited invention. Claims 14-16, as dependent from Claim 13, are indefinite for the same reason.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Rejection of Claims 12-16 under 35 U.S.C. 112, first paragraph/enablement, for the reasons explained in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the following arguments.

(A) The invention relates to a method of using S6 kinase 1 (S6K1) inhibitors in a new method. S6K1 is already known in the art as a potential target in caner and angiogenesis. S6K1 inhibitors were also known in the art at the time of filing. The specification provides clear guidance on how to identify S6K1 inhibitors without undue burden.

(B) The scope of the method is limited. Weight disorder is defined specifically in the claims as related to a disorder dependent on fat accumulation. The S6 kinase activity is defined in the new claim as S6K1 activity.

(C) The present invention is based upon the findings that S6K1 deficient mice show a reduction in white fat and brown fat, due to a reduction in a fat cell size, and that $S6K1^{-/-}$ mice are protected against fat accumulation, due to a sharp increase in basal lipolysis and a highly elevated metabolic rate. The correlation between S6K1 activity is not only shown using knockout mice having no S6K1 activity (Examples 1-8) but also shown with (i) adipose tissue

data from obese and normal mice tissue and (ii) obesity model mice with elevated S6K1 activity (see Example 9).

(D) This correlation between fat accumulation and S6K1 activity would indicate to one of skill in the art that inhibitors of S6K1 would find use in e.g., diagnosis or treatment of any disorders resulting in fat accumulation. The claimed use has been asserted by in vivo data in animal model; the claimed use could only be further evaluated in a clinical trial. An applicant for a patent is not required to provide results from human clinical trials.

These arguments are not found to be persuasive for the following reasons.

(A) Reply: It is acknowledged that the claims are so directed, that the human and mouse S6K1 are known in the art, that some mammalian S6K1 proteins have been implicated in cancer and angiogenesis, that some S6K1 inhibitors are known, and that some methods for identifying inhibitors of some S6K1 proteins are also known. However, the claims are directed to a method using any inhibitor of any S6K1 protein. The specification states:

> '"S6K" or "S6 kinase" is used herein to encompass both S6K1 (p70 and p85) and S6K2 (see, for example, Genebank Accession No. M57428, AJ007938, AB019245, NM003952 and related sequences), although S6K1 is a preferred target. Exemplary functional equivalents (variants) or derivatives of S6K include molecules where S6K is covalently modified by substitution, chemical, enzymatic, or other appropriate means with a moiety other than a naturally occurring amino acid.' [0021]
>
> and
>
> "S6 kinase is a kinase that phosphorylates the ribosomal protein, S6. Deletion of the S6K1 gene (also known as p70/p85 S6K) in mice led to the identification of an S6K1 homologue, S6K2, which can partly compensate for S6K1 function biochemically to phosphorylate S6 (Shima et al., 1998, EMBO J., 17, 6649-6659)." [0004]

Thus, the term S6K1 encompasses any protein, having any structure, wherein the protein can have a variety of activities, including phosphorylation of the S6 ribosomal protein. The specification fails to enable the skilled artisan to make all said S6K1 proteins, use all said S6K1

proteins to identify inhibitors of any function thereof, or use all said identified inhibitors for successful treatment of a weight disorder.

(B) Reply: It is acknowledged that weight disorder is defined in the claims as specifically dependent on fat accumulation. However, see (A), above, and the rejections under 35 U.S.C. 112, second paragraph.

(C) Reply: It is acknowledged that S6K1 deficient mice have a reduction in white and brown fat, a reduction in a fat cell size, an increase in basal lipolysis, and possibly an elevated metabolic rate. However, said findings do not enable the skilled artisan to make all S6K1 proteins having any structure, use all said S6K1 proteins to identify inhibitors of any function thereof, or use all said inhibitors for successful treatment of a weight disorder. In addition, Applicants' assertion of a correlation between S6K1 phosphorylation of S6 and obesity is not found to be persuasive in light of the prior art. As taught by Shima et al, S6 phosphorylation is normal in $S6K1^{-/-}$ mice (Fig 4), the same mice taught by the specification (pg 30, parg 1). Thus, the slow growth in $S6K1^{-/-}$ mice is not due to inhibition of S6 phosphorylation by S6K1 kinase, but inhibition of some other function of S6K. Neither the specification nor the prior art have identified said other function of S6K, any methods for identifying inhibitors thereof, or any methods of using any said identified inhibitor for treating obesity.

(D) Reply: It is acknowledged that there is a correlation between the expression of S6K1 and obesity in the mouse. It is also acknowledged that, depending on the ability to reach the desired cellular target in vivo, some inhibitors of mouse S6K1 may be useful for treating or preventing obesity in the mouse. However, neither the specification nor the prior art provide

evidence as to which inhibitors of which function(s) of any S6K1 can be used to successfully treat or prevent obesity in any living organism. Also see (C), above.

For these reasons and those explained in the prior action, rejection of Claims 12-16 under 35 U.S.C. 112, first paragraph/enablement, is maintained.

Written Description

Rejection of Claims 12-16 under 35 U.S.C. 112, first paragraph/written description, for the reasons explained in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants provide the same arguments stated above for lack of enablement.

The arguments are not found to be persuasive for the following reasons.

(A) Reply: The instant claims are directed to methods using the genus of any inhibitor of any S6K1 protein, having any structure and any function, including phosphorylating the S6 ribosomal protein. The specification fails to describe said methods in a manner to convey that the inventors were in possession of the invention at the time of filing.

(B) Reply: See (A), above.

(C) Reply: Said finding do not described how to make all S6K1 proteins having any structure, use all said S6K1 proteins to identify inhibitors of any function thereof, or use all said inhibitors for successful treatment of a weight disorder. The recited invention has not been described in a manner to convey that the inventors were in possession of the invention at the time of filing.

(D) Reply: The specification fails to describe methods for successfully using all inhibitors of any S6K1 to treat or prevent obesity in any living organism, in a manner to convey that the inventors were in possession of the invention at the time of filing.

For these reasons and those explained in the prior action, rejection of Claims 12-16 under 35 U.S.C. 112, first paragraph/written description, is maintained.

Claims 14-16 are herein further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 14-16 are directed to a genus of methods for treating a weight disorder using an S6K1 inhibitor, wherein the S6K1 inhibitor binds to the ATP binding site of S6K1, binds to the catalytic domain of S6K1, or is an antibody, respectively. The specification teaches no such methods. Given this lack of description of representative species encompassed by the genera of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 12 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Shima et al, 1998. Shima et al teach a method for inhibiting S6K1 in mice by inactivating the encoding gene

(Fig 1). The method of Shima et al is identical to the method disclosed by the specification (Example 1; pg 30, parg 1). Therefore, Claims 12 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Shima et al, 1998.

Allowable Subject Matter

No claims are allowable.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 571-272-0943. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashed can be reached on 571-272-092834. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published application may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on the access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Sheridan Swope/
Primary Examiner, 1652